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| EXAMINER | |
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| **ART UNIT** | **PAPER NUMBER** |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/574,911 | AITKEN ET AL. | |
| | Examiner | Art Unit | |
| | ALEX NOGUEROLA | 1795 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *10 March 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-24 and 27-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-24 and 27-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Response to Arguments*

1. Applicant's arguments with respect to claims 1-24 and 27-29 have been considered but are moot in view of the new grounds of rejection.

### *Status of the Rejections pending since the Office action mailed on September 10, 2009*

2. All previous rejections are withdrawn.

***Claim Rejections - 35 USC § 102***

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-3, 6, 7, 12, 13, 17, 20, and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by an English language translation of CN 89105110.4 (hereafter "Su").

Addressing claim 1, Su discloses a process for separating a sperm type from a sperm population in a sperm sample by electrophoresis (claim 1) comprising subjecting the sperm population to an electric potential such that a sperm type is separated from a sperm population through an ion-permeable barrier. See the last paragraph on page 4 of Su. The Examiner construes the "semi-permeable bag" of Su as the claimed "ion-permeable barrier" because Su states, "Due to the separation method of this invention, the design of the electrophoresis cell used can prevent direct contact between the semen and the electrodes while also supporting the spermatozoa's source of energy without affecting the spermatozoa." See the tip of page 5. If the semi-permeable bag were not permeable to ions then electrolyte would be blocked and electrophoresis field disrupted.

Addressing claims 2 and 3, Su discloses at least separating sperm type having a certain gender and robustness or fertilizing potential (e.g., "In the results of ten

experiments on X spermatozoa from semen by the method of this invention, the average value was 91.79 ± 6.4, with vitality of 0.68 ± 0.18." See bottom of page 6.

Addressing claim 6, the semen sample explicitly contains X-sperm and implicitly Y-sperm.

Addressing claims 7, 20, and 21, for the additional limitations of these claims see the bottom of page 6 ("In the results of ten experiments on X spermatozoa from semen by the method of this invention, the average value was 91.79 ± 6.4, with vitality of 0.68 ± 0.18.").

Addressing claims 12 and 13, for the additional limitations of these claims see the last paragraph on page 4 ("... at a voltage 3V and a current of 40-100 μA, ...")

Addressing claim 17, for the additional limitation of this claim see page 6 ("The semen was diluted with 3.9 mL of diluant.")

***Claim Rejections - 35 USC § 103***

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1, 5-10, 12, 13, and 17-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moore et al. "Isoelectric Focusing of Boar Spermatozoa," *J. Reprod. Fert.* (1975) 44, 329-332 (hereafter "Moore"), Speicher et al. US 6,638,408 B1 (hereafter "Speicher").

Addressing claim 1, Moore discloses a process for separating a sperm type from a sperm population in a sperm sample by electrophoresis (abstract and Figure 1) comprising subjecting the sperm population to an electric potential such that a sperm type is separated from a sperm population through a pH-gradient (abstract; Figure 1; and last paragraph on page 329, bridging to page 330). Moore does not mention providing an ion-permeable membrane in the isoelectric focusing device.

Speicher discloses a method and device for separation of charged molecules by solution isoelectric focusing. The device comprises a separation chamber having an electrode at each end thereof between which is a series of ion-preamble membranes spaced apart in sequence that partition the chamber into regions having a preset pH range. See the abstract; Figures 1, 8, and 9; col. 04:56 - col. 05:17; and col. 06:17-31. It would have been obvious to one with ordinary skill in the art at the time of the invention to substitute the isoelectric focusing device of Speicher for that used by Moore in Moore's method because the isoelectric device of Speicher does not require a large sample volume; does not produce large volume, dilute fractions that need to be concentrated with attendant loses; has very good resolution; and does not require

expensive, complex instrumentation. See Speicher col. 02:30-37. Additionally, the device of Speicher would be easier to prepare than that of Moore because a pH density solution (ficoll density gradient) does not have to be prepared as instead solid pH membranes are used. As such, the isoelecric focusing device of Speicher potentially offers much better separation than the device of Moore because the pH intervals in Speicher can be much more easily controlled just by adjusting the number of, thicknesses of, and spacing between the pH membrane, rather than trying to distribute the Ampholines in the ficoll density into very narrow bands. See col. 06:04-61 and col. 07:12-17. Furthermore, sample recovery is also much easier with the isoelectric focusing device of Speciher than with that of Moore. Compare col. 07:18-23 in Speicher with "Elution of the gradient was by way of a 'flow-through' pH electrode" and "The gradient containing the focused spermatozoa was run from the column through a 0.5 ml 'flow-through' pH electrode connected to a pH meter ..." as discussed in the Figure 1 caption and top paragraph on page 330 of Moore. Finally, Applicant should note that although Speicher mostly describes using the isoelectric focusing device with samples of protein mixtures, Speicher does discloses that the samples may be biological fluids or cell or tissue samples. See col. 10:33-37. Thus, to use the isoelectric focusing device of Speicher to practice the method of Moore (that is substituting the Perspex column and ficoll pH gradient of Moore with the isoelectric focusing device of Speicher having equivalent or even narrower pH intervals and still using the same electrode solutions and sample) is just substitution of one known device for another with predictable results.

Addressing claim 5, for the various claimed sample chambers, electrolyte chambers, and ion-permeable barriers see Figures 1, 8, and 9 in Speicher.

Addressing claim 6, Moore used at least spermatozoa from intact boars and spermatozoa from vesiculectomized boars. See the last paragraph on page 330.

Addressing claim 7, for the additional limitation of this claim see Figure 2 in Moore, for example.

Addressing claims 8-10, for the additional limitations of these claims see in Speicher col. 05:36-54, which discloses that a range of range of small diameter pore sizes could be used. Barring a contrary showing, such as unexpected results, the choice of pore size is just optimization of the separation. As for the ion-permeable barriers being "electrophoresis membranes", since they are being used in an electrophoresis device they are "electrophoresis membranes". Moreover, Speicher discloses making the membranes from a variety of materials including polyacrylamide, agarose, or polyacrylamide-agarose. See col. 05:55-61.

Addressing claim 12, although Moore does not mention any voltage range Speicher discloses using 100 V and 200 V to separate cellular material. See col. 16:29-44. Thus, barring a contrary showing, such as unexpected results to carry out the electrophoresis within the claimed voltage is range is optimization of known result effective separation variable.

Addressing claim 13, for the additional limitation of this claim see page 330 of Moore, which discloses applying a 2 mA current during electrophoresis.

Addressing claim 17, for the additional limitation of this claim note that Moore discloses diluting the sperm in the pH gradient ("Spermatozoa from intact and vesiculectomized boars …resuspended in 0.3 ml of the pH/ficoll gradient removed from the Colum …" – bottom of page 329, bridging to page 330) thus Moore implicitly discloses diluting the sperm in a buffer, although molar concentration of the buffer is not clear. However, barring a contrary showing, such as unexpected results, selecting the buffer concentration is just a matter of optimization especially in an isoelectric focusing device.

Addressing claims 18 and 19, the sperm sample concentration in Moore is 5 x $10^6$ / 0.3 ml, which is about 18.6 x $10^{6/}$ ml, which is within both the claimed ranges.

9. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Moore as modified by Speicher as applied to claims 1, 5-10, 12, 13, and 17-19 above, and further in view of Barbour et al. US 5,436,00 (hereafter "Barbour").

Although Speicher does not appear to mention polycarbonate as a membrane material Speicher does discloses that a variety of materials could be used including synthetic and natural polymers and glass. Speicher also discloses that the pore size may be as small as 0.5 microns. See col. 05:55-65. As shown by Barbour polycarbonate membranes with a pore size of 3 μm were used in biochemical experiments on cells at the time of the invention. See the abstract and col. 15:21-25. Thus, barring a contrary showing, such as unexpected results, to have the membrane be made of polycarbonate and have a pore size within the claimed range is just use of known membrane material and pore size in related biochemical/biological arts for optimizing the sperm separation during electrophoresis.

10. Claims 2, 3, and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moore in view of Speicher as applied to claims 1, 5-10, 12, 13, and 17-19 above, and further in view of Moore "The Net Surface Charge of Mammalian Spermatozoa as

Determined by Isoelectric Focusing, Changes Following Sperm Maturation, Ejaculation, Incubation in the Female Tract, and after Enzyme Treatment" International Journal of Andrology 2 (1979) 449-452 (hereafter "Moore II").

Addressing claims 2 and 3, arguably Moore already discloses at least separating sperm type having fertilizing potential since normal boar spermatozoa could be differentiated by isoelectrophoresis from spermatozoa from boar without seminal vesicles. See the Moore abstract. In any event, Moore II teaches that with isoelectric focusing "... a preliminary study showed that spermatozoa from some apparently infertile men have an isoelectric point consistently higher than those from fertile men." See page 449. Thus, in light of Moore II to use the process of Moore as modified by Speicher to separate sperm based on fertilizing potential is an obvious variant that would be clearly useful in determining and diagnosing infertility.

11. Claims 14 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moore in view of Speicher as applied to claims 1, 5-10, 12, 13, and 17-19 above, and further in view of Jaspers et al. "Separation of Bacterial Cells by Isoelectric Focusing, a New Method for Analysis of Complex Microbial Communities," Applied and Environmental Microbiology, Aug. 1997., p. 3176-3181 (hereafter "Jaspers") and Raptis US 6,001,617 (hereafter "Raptis"), Burke, Jr. et al. US 2002/0119218 A1 (hereafter "Burke")

Addressing claims 14 and 15, Moore does not appear to mention the voltage gradient applied during electrophoresis. However, barring a contrary showing, such as unexpected results, adjusting the voltage gradient is just optimization of a known result effective variable. As was known in the art at the time of the invention the higher the electrophoresis voltage the faster the separation; however, this gain is offset by increased heating of the electrophoresis solution, which may distort the separation. In fact, too high a voltage gradient, which may porate, fuse, injure, or even kill living cells. See, for example, Raptis col. 02:60-65; Burke the abstract and specification paragraph [0011]. It was also known at the time of the invention to use a voltage gradient of 11.5 V/cm for isoelectrophoresis of living whole bacterial cells, which would further suggest to one of ordinary skill in the art at the time of the invention to use a low voltage gradient, such as within the claimed ranges. See the Jaspers abstract and the second column on page 3179.

12. Claims 1-10, 12-23, 28, and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Engelmann et al. "Separation of Human X and Y Spermatozoa by Free-Flow Electrophoresis," Gamete Research 19:151-159 (1988) (already of record, hereafter "Engelmann") in view Weber US 7,3999,394 B2 (hereafter "Weber")

Addressing claim 1, Engelmann discloses a process for separating a sperm type from a sperm population in a sperm sample by free-flow electrophoresis (abstract) comprising subjecting the sperm population to an electric potential such that a sperm type is separated from a sperm population through a buffer medium (abstract). Engelmann does not mention providing an ion-permeable membrane in the isoelectric focusing device.

Weber discloses a free-flow electrophoresis method and device for separating charged substances in which sample components pass through one or more ion-permeable membranes (2) arranged parallel to the electrodes (4). See the abstract; Figures 3-6; and col. 03:38-47. It would have been obvious to one with ordinary skill in the art at the time of the invention to provide ion-permeable membranes as taught by Weber in the invention of Engelmann because as taught by Weber this will enhance sample separation by combining electrofiltration with free-flow fractionation in a way that avoids overheating of the fluid in the device, yet allows increased sample throughput at high speed. See col. 01:17 - col. 02:40; and col. 05:15-45.

Addressing claims 2-4, Engelmann discloses at least separating sperm type based on motility, robustness, fertilizing potential, or gender (the Examiner construes "viability" in Engelmann to encompass robustness and fertilizing potential). See the abstract, Y-Chromatin Distribution Before and After Separation on page 154, and Viability and Motility of Separated Spermatozoa on page 156.

Addressing claim 5, for the various claimed sample chambers, electrolyte chambers, and ion-permeable barriers see Figure 6 in Speicher.

Addressing claim 6, Engelmann used at least X-sperm/ Y-sperm, viable sperm/non-viable sperm, and motile sperm/ low motility sperm. See pages 153 and 156.

Addressing claim 7, for the additional limitation of this claim see in Engelmann Figure 2 and Table 1, for example.

Addressing claims 8-10, for the additional limitations of these claims consider that Weber discloses using the membranes for electrofiltration, which clearly suggests that the pore size would be pre-selected. This also clearly stated in col. 03:55-57: "The material and the pore size of the hollow fiber 2 differ according to the application concerned, i.e., the samples to be treated, and are chosen accordingly." With multiple membranes as shown in Figure 6 they clearly do not all have to have the same pore size. For claim 9 note that since the membranes in the device used in the process of Engelmann as modified by Weber is an electrophoresis device, the membranes are "electrophoresis membranes" in addition to being ion-permeable membranes.

Addressing claims 12 and 14 for the additional limitation of this claim see in Engelmann Electrophoresis: Operating Conditions on page 153.

Addressing claim 13, Engelmann as modified by Weber does not appear to mention a current or current range during electrophoresis; however, barring a contrary showing, such as unexpected results, adjusting the current is just a matter of adjusting a known result-effective variable for optimization of the separation. If the current is too high, which would primarily be due to the voltage gradient and the conductivity of the electrophoresis solution, then there may be overheating, which would adversely affect the separation. Also, too high a current may actually kill the sperm cells. On the other hand, too low a current suggests too low a voltage and too slow a separation.

Addressing claim 15, Engelmann only mentions a voltage gradient of 80-120 V/cm. See Engelmann Electrophoresis: Operating Conditions on page 153. However, Engelmann states, "The velocity of the chamber buffer flow was adapted to each individual sample and the selected electric current." *ibid.* The voltage gradient will largely decide the current along with conductivity of the electrophoresis solution. One with ordinary skill in the art at the time of the invention would recognize that the voltage gradient could be reduced, but at the cost of increasing the separation or adversely

affecting the quality of the separation. Thus, barring a contrary showing, especially since no other operational parameters are claimed, to reduce the voltage gradient from 80 V/cm as already taught by Engelmann to 16 to 20 V/cm as claimed will have predictable results.

Addressing claim 16, Engelmann discloses an electrophoresis time of 80 seconds. As for the sample size it must be very small, such as that claimed, because the separation chamber is only 120 x 30 x 0.3 mm. See Electrophoresis: Operating Conditions on page 153 and Free-Flow Electrophoresis on page 152.

Addressing claim 17, Engelmann states, "Briefly, the ejaculate was diluted twofold with Hanks' solution (Boehringer Mannheim, buffered with HEPES 10 mM, ..."). See Buffer Systems on page 152.

Addressing claims 18 and 19, Engelmann states, "... to give a final sperm density of approximately 60-80 x $10^6$ /ml." See Free-Flow Electrophoresis on page 152.

Addressing claims 20-23 and 29, Engelmann states, "On the other hand, the viability determined by eosin staining, exhibited only an insignificant decrease after the

separation procedure. The viability in the different fractions remained approximately the same when compared with their original values before separation (Fig. 3)." See Viability and Motility of Separated Spermatozoa on page 156.

Addressing claim 28, although Engelmann found reduced motility for each sperm fraction (Viability and Motility of Separated Spermatozoa on page 156), the fractions were, still motile (Figure 3 for example has a lowest motility between 5-10%). In regard to this claim, it should be kept in mind that Applicant did not measure a change in motility other than whether the sperm moved or did not move: "Slides were scored immediately after preparation, with *any directional movement* of cells being *classified as motile* in contrast to totally immotile sperm. [emphasis added]" See Applicant's specification page 12, lines 5-11. In contrast, Engelmman still found sperm movement, albeit reduced.

13. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Engelmann as modified by Weber as applied to claims 1-10, 12-23, 28, and 29 above, and further in view of Barbour.

Although Weber does not appear to mention particular membrane materials, especially polycarbonate, nor pore sizes, Weber states: "The material and the pore size of the hollow fiber 2 differ according to the application concerned, i.e., the samples to be treated, and are chosen accordingly." As shown by Barbour polycarbonate membranes

with a pore size of 3 μm were used in biochemical experiments on cells at the time of the invention. See the abstract and col. 15:21-25. Thus, barring a contrary showing, such as unexpected results, to have the membrane be made of polycarbonate and have a pore size within the claimed range is just use of known membrane material and pore size in related biochemical/biological arts for optimizing the sperm separation during electrophoresis.

14. Claims 18 and 19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Su in view of Christensen et al. US 7,070,917 B1 (hereafter "Christensen").

Su discloses a process for separating a sperm type from a sperm population in a sperm sample by electrophoresis (claim 1) comprising subjecting the sperm population to an electric potential such that a sperm type is separated from a sperm population through an ion-permeable barrier. See the last paragraph on page 4 of Su. The Examiner construes the "semi-permeable bag" of Su as the claimed "ion-permeable barrier" because Su states, "Due to the separation method of this invention, the design of the electrophoresis cell used can prevent direct contact between the semen and the electrodes while also supporting the spermatozoa's source of energy without affecting the spermatozoa." See the tip of page 5. If the semi-permeable bag were not permeable to ions then electrolyte would be blocked and electrophoresis field disrupted.

Su mentions that the original bovine semen density was 1.3 billion without units, so it is not known whether this value would fall within the claimed ranges if in the same units. However, Christensen, which discloses a device for counting sperm, discloses that a bovine sperm count within the claimed ranges would not be unexpected. See the abstract; col. 9:40-52; and col. 12:54-67. So, barring a contrary showing by Applicant, one with ordinary skill in the art would expect similar results using the process of Su with bovine sample in the claimed ranges, especially if the electrophoresis parameters were slightly adjusted, if need be.

15. Claim 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over Su in view of Kricka et al. US 5,427,946 ("hereafter "Kricka").

Su discloses the process of claim 1. Su discloses a process for separating a sperm type from a sperm population in a sperm sample by electrophoresis (claim 1) comprising subjecting the sperm population to an electric potential such that a sperm type is separated from a sperm population through an ion-permeable barrier. See the last paragraph on page 4 of Su. The Examiner construes the "semi-permeable bag" of Su as the claimed "ion-permeable barrier" because Su states, "Due to the separation method of this invention, the design of the electrophoresis cell used can prevent direct contact between the semen and the electrodes while also supporting the spermatozoa's source of energy without affecting the spermatozoa." See the tip of page 5. If the semi-

permeable bag were not permeable to ions then electrolyte would be blocked and electrophoresis field disrupted.

Su does not specifically mention fertilizing an ovum with sperm separated by the process of claim 1; however, it would have been obvious to one with ordinary skill in the art to do so because the natural function of viable sperm is to fertilize an ovum. Moreover, as shown by Kricka it was known in the art at to use sperm separated in a small scale analytical device to fertilize an ovum. See Kricka the abstract.

16. Claim 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over Engelmann as modified by Weber as applied to claims 1-10, 12-23, 28, and 29 above, and further in view of Kricka.

Engelmann as modified by Weber does not specifically mention fertilizing an ovum with sperm separated by the process of claim 1; however, it would have been obvious to one with ordinary skill in the art to do so because the natural function of viable sperm is to fertilize an ovum. Moreover, as shown by Kricka it was known in the art at to use sperm separated in a small scale analytical device to fertilize an ovum. See Kricka the abstract.

17. Claim 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over Moore as modified by Speicher as applied to claims 1, 5-10, 12, 13, and 17-19 above, and further in view of Kricka.

Moore as modified by Speicher does not specifically mention fertilizing an ovum with sperm separated by the process of claim 1; however, it would have been obvious to one with ordinary skill in the art to do so because the natural function of viable sperm is to fertilize an ovum. Moreover, as shown by Kricka it was known in the art at to use sperm separated in a small scale analytical device to fertilize an ovum. See Kricka the abstract.

***Claim Rejections - 35 USC § 112***

18. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

19. Claim 2 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for separating sperm based on motility, robustness, gender, and fertilizing potential does not reasonably provide enablement for separating sperm based on genetic makeup or morphological normality. The specification does not

enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with this claim.

Genetic makeup is determined by chromosomes contained within the sperm cell. More particularly it is the DNA sequence of the chromosomes that determines genetic makeup ("Each gene has its own specific location on the chromosome and is a piece of genetic material that does one particular job. All of the 20,000 or so genes contain a different 'packet' of information necessary for out bodies to grow and work. Our genes also contain the information for how we look: the colour of our eyes, how tall we are, the shape of our nose, etc. The information is in the form of a chemical (DNA) code (the genetic code) .."). See the "Genes and Chromosomes" article produced by the Centre for Genetics Education, especially page 4. The Examiner is not aware of any correlation between sperm movement under electrophoresis and the DNA sequence of chromosomes therein. Indeed, it would be most astounding if the DNA sequence of chromosomes could be sequenced intact in sperm simply by moving them with an electrical field through one or more membranes. Moreover, there does not appear to be any mention in the original specification of results of a genetic analysis of intact sperm by electrophoresis, let alone an example or suggestion as how to carry out such an analysis.

With regard to separating sperm based on morphological normality, Applicant's own specification discloses that Applicant has not been successful in such a separation. Figure 1 shows that at every electrophoretic time point comparable amounts of both groups of sperm appeared. Indeed, Applicant found "... normal morphology in the

separated fraction (35±1.2%) compared to that of the excluded fraction (28±4%) …" 35% - 1.2% = 33.8%. 28% + 4% = 32 %. 33.8% - 32% = *1.8%,* which is not a significant difference. See page 15 of the specification. Moreover, the sperm underwent considerable chemical and biochemical processing after being collected at the different electrophoresis time points. See Sperm Morphology, which begins on page 13 of the specification. It would seem, therefore, that the electrophoresis had little if any role in distinguishing sperm based on morphological normality.

For these reasons undue experimentation would be required to practice the invention of claim 2 for genetic make-up and morphological normality, so Applicant's disclosure does not enable "genetic makeup" and "morphological normality" in claim 2.

20. Claim 4 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for separating sperm based on poor motility, does not reasonably provide enablement for separating sperm based on poor morphology, high levels of DNA damage, and high levels of reactive oxygen species generation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with this claim.

The issue of enablement with respect to separating sperm by motility has already been addressed above in the rejection of claim 2 under 35 U.S.C. 112, first paragraph. So those arguments will also apply here without being repeated.

With regard to separating sperm based on high levels of DNA damage, Figure 3 purports to show some sort of separation of sperm with damaged DAN from sperm with undamaged DNA. See page 5. However, the greatest separation in the two groups occurred at time zero, presumably before electrophoresis even began. Additionally, the absolute and relative amounts did not vary much over time when one considers that the tallest bar is not over 10%. As for the claim in claim 2 of being able to separate sperm based on genetic make-up, it would be remarkable DNA damage of DNA in intact living sperm cold be detected just by using an electric field to move them one or more membranes.

With regard to separating sperm based on high levels of reactive oxygen species generation. Results shown in Applicant 's Figure 4 do not show clear separation of sperm with high level of reactive species oxygen species generation from sperm without high levels of reactive oxygen species generation *using electrophoresis*. Indeed, the greatest separation appears at time 0 (zero), before electrophoresis. Also, the samples collected at the different time points underwent considerable mechanical, chemical, and biochemical processing *after* the electrophoresis. See Acrosmoe Reactions on page 14 of the specification. So, electrophoresis seems to have played little role in the sperm separation based on levels of reactive oxygen species generation.

21. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ALEX NOGUEROLA whose telephone number is (571) 272-1343. The examiner can normally be reached on M-F 8:30 - 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, NAM NGUYEN can be reached on (571) 272-1342. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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/Alex Noguerola/

Primary Examiner, Art Unit 1795

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